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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,448	11/07/2001	David Lewis	Mirus.030.03	3784

7590 11/23/2004

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EXAMINER	
GIBBS, TERRA C	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 11/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/007,448	LEWIS ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2004 and 30 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9 and 13-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9 and 13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicants Terminal Disclaimer, Applicants declaration under 37 C.F.R. 1.131, Applicants Amendment and Remarks filed July 30, 2004, and Applicants Petition and Amendment filed August 19, 2004.

Claims 10-12 have been canceled. Claim 1 has been amended.

Claims 1, 3-9, and 13-16 are pending in the instant application.

Claims 1, 3-9, and 13-16 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Terminal Disclaimer

The terminal disclaimer filed July 30, 2004 has been considered by the Examiner and is approved.

Specification

Applicant's amendment to the specification is acknowledged. It is noted that this patent application claims the benefit of provisional applications 60/315,934, filed August 27, 2001, and 60/324,155, filed September 20, 2001; and is a Continuation-in-Part of applications 09/707,117, filed November 6, 2000 and 09/877,436, filed on June 7, 2001, which is a divisional of 09/450,315 filed Nov. 29, 1999, now Patent No. 6,379,966, claims priority of provisional applications 60/121,730 filed on Feb. 26, 1999, and 60/146,564 filed on Jul. 30, 1999.

It is noted that the instant claims have been granted priority to July 30, 1999.

Claim Rejections - 35 USC § 112

In the previous Office Action mailed June 16, 2004, claim 1 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This rejection is withdrawn** in view of Applicants amendment to the claims to correct for antecedent basis.

Double Patenting

In the previous Office Action mailed June 16, 2004, claims 1, 3-5, 8, 13, and 15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over 1, 2, 6, 7, and 8 of U. S. Patent No. 6,379,966 ('966). **This rejection is withdrawn** in view of Applicants filing of a terminal disclaimer.

Claim Rejections - 35 USC § 102

In the previous Office Action mailed June 16, 2004, claims 1, 3-6, 8, 13, 15, and 16 were rejected under 35 U.S.C. 102(b) as being anticipated by Makino et al. (Hypertension, 1998 Vol. 31:1166-1170). **This rejection is withdrawn** in view of Applicants amendment to the claims to recite, "inserting a polynucleotide, which is not complexed with another molecule". It is acknowledged that Makino et al. discloses an oligonucletoide complexed with poly(L)lysine. It is further noted that in addition to amending the claims, Applicants argue that the specification has been amended to include parent applications that pre-date the Makino reference. This did not persuade the Examiner because the instant claims have been awarded priority to July 30,

1999. The Makino reference was published May 31, 1998. Since the Makino reference was published more than one year prior to the filing date of the instant invention, it would apply as art under 35 USC 102(b). It is also noted that Applicants provided a §1.131 Declaration to establish invention for delivery of short polynucleotides prior to the effective dates of the cited references. This did not persuade the Examiner because a §1.131 Declaration is appropriate when the reference is not a statutory bar under 35 USC 102(b) (c) or (d). As indicated above, the Makino reference was published more than one year prior to the filing date of the instant invention, and would therefore apply as art under 35 USC 102(b).

In summary, only Applicants amendment to the claims to recite "inserting a polynucleotide, which is not complexed with another molecule" has persuaded the Examiner to withdrawn the 35 U.S.C. 102(b) rejection against claims 1, 3-6, 8, 13, 15, and 16 as being anticipated by Makino et al.

In the previous Office Action mailed June 16, 2004, claims 1, 3-5, 9, 13, 14, and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Wianny et al. (Nature Cell Biology, 2000 Vol. 2:70-75). **This rejection is withdrawn** in view of Applicants Amendment to the claims to recite "wherein the vessel consists of arteries, arterioles, capillaries, venules, sinusoids, veins, lymphatics, and bile ducts" and in view of Applicants petition under 37 CFR §1.78(a)(3) to include parent applications that pre-date the Wianny reference. It is noted that Wianny et al. disclose injecting into the uteri of mice.

In summary, Applicants amendment to the claims to recite "wherein the vessel consists of arteries, arterioles, capillaries, venules, sinusoids, veins, lymphatics, and bile ducts" and

Applicants petition under 37 CFR §1.78(a)(3) has persuaded the Examiner to withdrawn the 35 U.S.C. 102(b) rejection against claims 1, 3-5, 9, 13, 14, and 15 as being anticipated by Wianny et al.

In the previous Office Action mailed June 16, 2004, claims 1 and 7 were rejected under 35 U.S.C. 102(e) as being anticipated by Kay et al. [U.S. Patent No. 6,107,027]. **This rejection is withdrawn** in view of Applicants amendment to the claims to recite, "inserting a polynucleotide, which is not complexed with another molecule". It is noted that Kay et al. disclose a recombinant adenovirus which encodes a ribozyme. It is further noted that in addition to amending the claims, Applicants provided a §1.131 Declaration to establish invention for delivery of short polynucleotides prior to the effective dates of the cited references. The §1.131 Declaration has persuaded the Examiner since a §1.131 Declaration can be used to overcome a reference when the reference is not a statutory bar under 35 USC 102(b) (c) or (d).

In summary, Applicants amendment to the claims to recite "inserting a polynucleotide, which is not complexed with another molecule" and Applicants §1.131 Declaration has persuaded the Examiner to withdraw the 35 U.S.C. 102(e) rejection against claims 1 and 7 as being anticipated by Kay et al.

Claim Rejections - 35 USC § 103

In the previous Office Action mailed June 16, 2004, claims 1, 3-5, 9, 10, 11, 12, 13, 14, and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over Wianny et al. (Nature Cell Biology, 2000 Vol. 2:70-75) in view of Caplen et al. (Proc Natl Acad Sci, 2001 Vol.

98:9742-7, Epub 2001 Jul 31). **This rejection is withdrawn** in view of Applicants Amendment to the claims to recite "wherein the vessel consists of arteries, arterioles, capillaries, venules, sinusoids, veins, lymphatics, and bile ducts" and in view of Applicants petition under 37 CFR §1.78(a)(3) to include parent applications that pre-date the Wianny reference. It is noted that Wianny et al. disclose injecting into the uteri of mice.

Applicant's amendment necessitated the new ground(s) of rejection presented below:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-9, and 13-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Claims 1, 3-9, and 13-16 are drawn to a process for delivering a polynucleotide into a cell of a mammal to inhibit protein expression comprising making the polynucleotide consisting of a sequence that is complementary to a nucleic acid sequence in the mammal, inserting the polynucleotide, which is not complexed with another molecule, into a vessel in the mammal, wherein the vessel consists of arteries, arterioles, capillaries, venules, sinusoids, veins,

lymphatics, and bile ducts, increasing the permeability of the vessel, and delivering the polynucleotide to the cell wherein the protein expression is inhibited.

Applicants contend that support for the phrase, "inserting the polynucleotide, which is not complexed with another molecule" can be found in each example where naked polynucleotides are used. However, the amended language, inserting a polynucleotide "which is not complexed with another molecule", cannot be found in the instant specification or claims as originally filed. The Examiner believes that the examples where naked polynucleotides are used provides an inherent characteristic of these polynucleotides not appreciated by Applicant at the time of filing, and therefore the skilled artisan would not recognize the limitation, inserting a polynucleotide "which is not complexed with another molecule" as a feature of the claimed invention as originally claimed. It is not readily apparent how the specific embodiment of examples where naked polynucleotides are used provides support for the language, inserting a polynucleotide "which is not complexed with another molecule." It is noted that the instant specification, at page 4, starting at line 25, expressly considers delivering naked DNA delivery. Given the delivery of naked DNA provided in the examples, along with the expressed disclosure beginning at page 4, starting at line 25, it appears that the instant specification has support for delivery of naked DNA, but not for the language, inserting a polynucleotide "which is not complexed with another molecule."

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1, 3, 4, 5, 6, 8, and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Kumasaka et al. (Journal of Clinical Investigation, 1996 Vol. 97:2362-2369).

Claim 1 is drawn to a process for delivering a polynucleotide into a cell of a mammal to inhibit protein expression comprising making the polynucleotide consisting of a sequence that is complementary to a nucleic acid sequence in the mammal, inserting the polynucleotide, which is not complexed with another molecule, into a vessel in the mammal, wherein the vessel consists of arteries, arterioles, capillaries, venules, sinusoids, veins, lymphatics, and bile ducts, increasing the permeability of the vessel, and delivering the polynucleotide to the cell wherein the protein expression is inhibited. Claims 3, 4, 5, 6, 8, and 13-15 are dependent on claim 1 and include all the limitations of claim 1, with the further limitations, wherein vessel permeability is increased by increasing pressure against vessel walls by increasing a volume of fluid within the vessel, wherein the vessel is a tail vein, wherein the cell is selected from a liver, spleen, heart, kidney, muscle or lung cells, and wherein the pressure increases extravascular volume.

Kumasaka et al. disclose a process for delivering a naked polynucleotide, ISIS 3082, into a cell of a mammal via intravenous injection. Kumasaka et al. disclose that ICAM-1 mRNA expression was detected and inhibited in the lung (see Figures 1 and 2). Kumasaka et al. disclose ISIS 3082 was injected into BALB/C mice through the tail vein and neutrophil emigration was

detected in the lungs (see Figure 4). It is noted that injection into the tail vein with ISIS 3082 is equivalent to increasing vessel permeability, by increasing pressure against vessel walls, increasing a volume of fluid within the vessel, and increasing extravascular volume as claimed because the method of intravascular injection would inherently increase pressure in the area of injection and at the time of injection. The pressure against the vessel walls would inherently be increased because the needle used is external to the tail vein. It is further noted that Kumasaka et al. are silent regarding the effects of ISIS 3082 on protein expression. However, given the inhibition of ICAM-1 mRNA expression by ISIS 3082, one of skill in the art would conclude that inhibition of protein expression would result, absent evidence to the contrary.

Therefore Kumasaka et al. anticipate claims 1, 3, 4, 5, 6, 8, and 13-15.

Claim 1, 3, 4, 5, 6, 8, and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Graham et al. (Journal of Pharmacology and Experimental Therapeutics, 1998 Vol. 286:447-458).

Claims 1, 3, 4, 5, 6, 8, and 13-15 are described above. Claim 16 is dependent on claim 1 and includes all the limitations of claim 1, with the further limitation wherein the vessel consists of liver.

Graham et al. disclose a process for delivering a naked polynucleotide, ISIS 1082, into a cell of a mammal via intravenous injection through the tail vein and the metabolism, pharmacokinetics, and intraorgan distribution in tissues such as the liver (see Figures 2-5, 11, and 12). It is noted that injection into the tail vein with ISIS 1082 is equivalent to increasing vessel permeability, by increasing pressure against vessel walls, increasing a volume of fluid

within the vessel, and increasing extravascular volume as claimed because the method of intravascular injection would inherently increase pressure in the area of injection and at the time of injection. The pressure against the vessel walls would inherently be increased because the needle used is external to the tail vein. It is further noted that Graham et al. are silent regarding the effect of ISIS 1082 on protein expression. However, given the quantitative pharmacokinetic information provided by Graham et al. following intravenous administration of ISIS 1082, one of skill in the art would conclude that inhibition of protein expression would result, absent evidence to the contrary.

Therefore Graham et al. anticipate claims 1, 3, 4, 5, 6, 8, and 13-16.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (571) 272-0758. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
November 18, 2004

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